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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,147	06/11/2001	Kenneth Kellar	NIDN-10	9771

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PATENT DEPARTMENT
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EXAMINER

HARTLEY, MICHAEL G

ART UNIT

PAPER NUMBER

1616

DATE MAILED: 08/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/830,147

Applicant(s)

KELLAR, KENNETH

Examiner

Michael G. Hartley

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6 and 10-20 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-4,6 and 10-20 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Art Unit: 1616

Response to Amendment

The preliminary amendment filed 6/11/01 has been entered. Claims 5, 7, 8, 9, 21 and 22 have been canceled. Claims 1-4, 6, 10-13, 15 and 19 have been amended.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification fails to describe the change in state in claim 6 "from a spherically symmetric electronic ground state to a non-spherically symmetric excited state" as now claimed. The specification only describes changes that start with a non-spherically symmetric electronic ground state, as set forth on page 4 of the specification. There is no mention of the change in state which is now set forth in the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6 and 10-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1 and 19, the phrase "preferably..." renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by

Art Unit: 1616

"such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. The same holds true for the recitation of "preferably" which follows the broad recitation.

Claim 6 recites the limitation "said change between two paramagnetic states" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

In claim 11, the recitation of "porphyrin-like" is indefinite because it is not clear how the term "like" modifies a porphyrin. The specification fails to define what is encompassed by "porphyrin-like" and/or how "like" differentiates over porphyrins. Thus, the scope of this recitation cannot be determined.

Also, in claim 11, the recitation of "chelates having a square planar symmetry" is indefinite because it is not clear what is encompassed thereby. The specification fails to define what chelates would be encompassed thereby and what is meant by this recitation. Thus, the scope of this recitation cannot be determined.

In claim 15, the recitation of "normal or abnormal biological processes" is indefinite because it is not clear what is encompassed thereby. There are an unlimited number of normal and abnormal biological process and the specification fails to define what is meant by this recitation. Thus, the scope of this recitation cannot be ascertained.

In claims 17 and 20, the recitation of "a redox agent" is indefinite. Since it is unclear what is being oxidized or reduced and given that various chemical moieties may act as oxidizing agent or reducing agents in various situations, this is not a term of art. Also, the specification fails to provide any definition of this term to define what types of compounds are useful as a "redox agent." Since it is unclear what types of chemical moieties are encompassed by a "redox agent" as used herein, this term is indefinite.

The dependent claims fall therewith.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

Art Unit: 1616

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 10, 12-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Garrity (WO 95/07270, relying on US equivalent, 5,958,373).

Garrity discloses a method of generating a contrast enhanced image of a human or non-human animal subject comprising administering a MRI contrast agent thereto, see abstract and column 11, lines 23+, see abstract. The chelates contain europium, as would be at once envisaged by one of ordinary skill in the art in reading the patent, see column 11, lines 27-32 and claim 8. The chelates include various polychelates of DOTA, DO3A, etc., as claimed, see column 2+. Note: the contrast agents “comprise” such chelates as set forth in claim 1, thus, would not exclude polychelates, as disclosed by Garrity. These are the same chelates that are used in the instantly claimed methods. The chelates are conjugated to a biological vector (e.g., an antibody, etc.) for *in vivo* targeting, see columns 9-10. The MRI contrast agents disclosed by Garrity include compositions having various additives, including antioxidants (i.e., a free radical scavenger), etc., see column 13.

Claims 1-4, 6, 10, 12, 15-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Platzek (US 5,277,895).

Platzek discloses a method of generating a contrast enhanced image of a human or non-human animal subject comprising administering a MRI contrast agent thereto, see abstract and column 11, lines 23+, see abstract and column 4, lines 33+. Platzek specifically discloses a europium chelate, see example 8, column 18. The chelates include DOTA compounds, etc., see column 3. The MRI contrast agents disclosed by Platzek include compositions having various additives, including antioxidants, such as, ascorbic acid (i.e., a free radical scavenger), etc., see column 9, lines 25-38.

Art Unit: 1616

Claims 1-4, 6, 11 and 13-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Sessler (US 5,599,923).

Sessler discloses a method of generating a contrast enhanced image of a human or non-human animal subject comprising administering a MRI contrast agent thereto, wherein the improvement is the use of a texaphyrin or porphyrin chelate, see abstract. The chelates contain metals europium, see pages column 4, lines 1-27. Given the limited number of metals, one of ordinary skill in the art would have at once envisaged the use of Eu as the metal contained therein. The porphyrin chelates are conjugated to a biological vector (e.g., an antibody, etc.) for *in vivo* targeting, see column 4, lines 28-36. Sessler also discloses the use of light in the methods, see column 10, lines 58-60.

Note: Since Garrity, Sessler and Platzek disclose methods which are the same as that instantly claimed, e.g., methods of MRI using the same chelates as instantly claimed, such chelates would inherently be expected to have the same properties as claimed, e.g., relaxivities, changes in oxidative states and/or relaxivities by biological processes, etc. It is noted that claims 15-18 do have active steps which require that an additional step is being performed. Also, the method of claim 1 does not include any activating step, but only the administration of a Eu chelate in a method of MRI, which is disclosed by the prior art. The same normal or abnormal biological processes, pH changes, etc. would occur upon the administration of the contrast agent of the prior art, which use the same contrast agents as claimed in methods of MRI having the same steps as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1616

Claims 1-4, 6, 10 and 12-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meade (WO 96/38184) in view of Hollister (US 5,801,228) in further view of Platzek (US 5,277,895).

Meade discloses a method of generating a contrast-enhanced image of a human or non-human animal subject comprising administering a MRI contrast agent thereto, see abstract. Meade discloses a method of MRI comprising administering metal chelates of DTPA, DOTA, etc., see page 17, lines 19+. These are the same chelates that are used in the instantly claimed methods. Meade further discloses that the contrast agents include a blocking group which acts as a trigger mechanism, which effectively changes the relaxivity state, see page 13, lines 4+, including enzymes, etc., see pages 24-26. The chelates include any paramagnetic metals useful for MRI, see page 15. The chelates are conjugated to a biological vector (e.g., an antibody, etc.) for *in vivo* targeting, see page 24.

Meade fails to specifically disclose that the chelates include europium complexes and include a free radical scavenger.

However, the use of europium as a paramagnetic metal in chelating agents for MRI contrast agents is well known in the art, as is the addition of a free radical scavenger as an additive.

Hollister teaches that europium is a well known metal species, which is equivalent to those employed by Meade, see column 6, lines 12-16.

Platzek teaches that Eu-chelates are useful for MRI, which dispersed in compositions containing various additives, such as, ascorbate (a free radical scavenger), see column 9, lines 25-38 and example 8(c).

It would have been obvious to one of ordinary skill in the art to modify the methods and compositions disclosed by Meade to use europium as the metal because it is well known in the art that europium is a useful paramagnetic metal species which is equivalent to other paramagnetic metal species for use in MRI, as shown by Hollister and Platzek. Further, it would have been obvious to one of ordinary skill in the art to include a free radical scavenger in the MRI compositions disclosed by Meade because such agents are well known as being additives to provide stable MRI compositions as shown by Platzek. Since the modification to Meade would yield the same metal chelates as claimed, and methods of MIR

Art Unit: 1616

using thereof, such chelates would inherently be expected to have the same properties as claimed, e.g., relaxivities, changes in oxidative states and/or relaxivities by biological processes, etc.

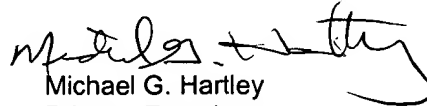
Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (703) 308-4411. The examiner can normally be reached on M-F, 7:30-5, off alternative Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose G. Dees can be reached on (703) 308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.


Michael G. Hartley
Primary Examiner
Art Unit 1616

MH
August 28, 2002